

Orals

Hand Dermatitis Secondary to Methylchloroisothiazolinone/methylisothiazolinone in Mechanics

Sonya J. Abdulla,¹ Melanie Pratt²

1. University of Ottawa, Ottawa, ON; 2. Division of Dermatology, University of Ottawa, Ottawa, ON

Background: Allergic contact dermatitis (ACD) is a common occupational disease and significant cause of work absenteeism. Dermatitis can be so severe that it will prompt vocational change. Methylchloroisothiazolinone/ methylisothiazolinone (MCI/MI, Kathon CG) is a common preservative found in waterless hand cleansers, many of which are used by mechanics. We present 9 cases of ACD secondary to MCI/MI evaluated at the Ottawa Patch Test Clinic over a 1-year period.

Objectives:

1. Examine the clinical features of ACD secondary to MCI/MI
2. Determine common sources of MCI/MI, particularly waterless hand cleansers used by mechanics
3. Discuss management options for mechanics with MCI/MI ACD
4. Determine the impact of contact allergen identification on the patient's quality of life, including vocational change

Methods: Patients underwent patch testing to the North American Contact Dermatitis Group Standard Screening Series, the chemotechnique oil & coolant series, rubber series plus other supplementary allergens in our mechanics series. Readings were performed at 48 and 96 or 120 hours. Follow-up interviews were conducted with patients in order to assess the impact of allergen identification on disease management and their quality of life.

Results: All patients had significant contact allergy to MCI/MI (>1+). The patient response to discontinuing waterless hand cleansers containing MCI/MI will be discussed.

Conclusions: MCI/MI is a common allergen found in waterless hand cleansers used by mechanics. MCI/MI allergen identification can direct disease management, allowing patients to improve their quality of life and avoid vocational change.

Cosmetic Concerns in Skin of Color

Andrew F. Alexis, St. Luke's-Roosevelt Hospital; Columbia University College of Physicians & Surgeons, New York, NY, USA

"Skin of color" refers to the broad range of skin types and complexions that characterize individuals of African, Asian, Latino, and Middle Eastern descent. Differences in structure, function, and cultural practices in individuals with ethnic skin contribute to variations in the prevalence and clinical presentation of numerous skin disorders. Understanding these differences is paramount in the treatment of darkly pigmented skin, especially in the context of cosmetic dermatology. In particular, numerous cosmetic procedures can be associated with disfiguring complications when the

nuances of treating pigmented skin are not taken into consideration. These complications include dyspigmentation, keloid scarring, and thermal injury. Safe and effective use of chemical peels, laser hair removal, fractional laser resurfacing and dermal filler injections in patients with skin of color will be discussed. Moreover, differences in the leading cosmetic concerns in populations with skin of color will be addressed.

308-nm Excimer Laser for the Treatment of Alopecia Areata

Nawaf Al-Mutairi, Kuwait University, Kuwait

Background: Alopecia areata is loss of hair from localized or diffuse areas of hair-bearing area of the skin. Recently there are reports of efficacy of the 308-nm excimer radiation for this condition.

Objective: To study the effect of the 308-nm excimer laser in the treatment of alopecia areata in children as well as adults with recalcitrant lesions.

Materials and Methods: Twenty-nine patients (adults and children) with 72 recalcitrant patches (including 1 adult and 2 children with alopecia totalis) were enrolled in this study. The lesions were treated with the 308-nm excimer laser twice a week for a period of 12 weeks; one lesion on each patient was left as a control for comparison.

Results: There were 14 males and 15 females in this study. None of the untreated control patches showed any regrowth of hair. Regrowth of hair was observed in 35 (48.6%) patches. Twenty-seven of the 40 (67.5%) scalp patches showed complete regrowth of hair. The extremity lesions failed to show a response. Atopic diatheses had an unfavorable effect on the outcome in our patients.

Conclusion: The 308-nm excimer laser is an effective therapeutic option for patchy alopecia areata of the scalp and for some cases with patchy alopecia areata of the beard area. It does not work for patchy alopecia areata of the extremities.

Trigeminal Port-Wine Stains: A Review of 304 Pediatric Cases and their Associated Complications

Isabelle Auger,¹ Catherine Maari,² Julie Powell,² Catherine McCuaig,²

1. CHUL du CHUQ, Québec, QC; 2. Ste-Justine Hospital, Montréal, QC

Objectives: To establish if the clinical pattern of skin involvement of facial trigeminal PWS can help to predict associated ocular and neurological features. To determine median age of apparition of complications, optimal duration of follow-up and investigation needed.

Design: Retrospective review of all cases of facial trigeminal PWS seen at Sainte-Justine Hospital's Dermatology Clinic, identified from 1992 to 2006. Examination of clinical photographs of PWS was done with documentation of distribution with special attention to the periocular area involvement defined as the "watershed area". We documented associated complications, mainly ophthalmologic and neurologic, as well as their age of onset.

Results: A total of 304 patients were included in the study. 253 patients had ocular and/or maxillary branches involvement. 186 patients had PWS adjacent to the eye. 29 patients (9.5% of the study population) had associated ocular or /and neurological complications.

Glaucoma was noted in 22 patients (7%) and neurological complications in 14 patients (4.6%). Patients with both ophthalmic and neurological complications tend to have multidermatomal implication with bilateral, extra-facial involvement and obligatory involvement of V1 or V2.

All the patients having either ophthalmologic or neurologic complications had “watershed area” involvement. Neuroradiologic investigation was realised for 75 patients having V1 or V2 stain. For 4 patients that eventually developed seizures, the CT-scan was initially normal in the first year of life. Remaining of patients with neurological complications had obvious radiological abnormalities. For 6 patients with no neurological (nor ocular) complications, significant abnormalities were noted at CT-scan or MRI.

Conclusions: We recommend that patients with a trigeminal PWS involving any part of the “watershed area” should be systematically investigated for ophthalmologic complications annually. For neurological investigation, an MRI should be recommended only in patients with periorbital involvement. The MRI can be negative in the first year of life and can show positive features in asymptomatic patients. If there is no involvement of the watershed area no investigation at all is necessary.

Top 8 Reasons Black Women are Losing their Hair: Exogenous and Endogenous Experience

Renée A. Beach, University of Ottawa, Division of Dermatology, Ottawa, ON

Black hair, for many dermatologists, remains an enigma. This may be due to a lack of patient encounters and exposure, a lack of knowledge regarding the literature in the field, or a combination of these two. This reality is complicated by the fact that black women present to dermatologists with hair pathology when, in many instances, the range of normalcy is not well-understood. Given the increasing presence of this demographic - dark-skinned women of African-Caribbean descent - in both urban and rural Canada, it is prudent for dermatologists to become more informed in this aspect of care.

This presentation will briefly summarize what is known about “black”, or afro-textured, hair in terms of its morphology and growth patterns according to the published academic literature. As well, using clinical cases to illustrate pathologic presentations, the main reasons why black women experience alopecia will be highlighted. Essentially, these can be grouped under exogenous or endogenous etiologies. Exogenous, or iatrogenic factors include hairstyles that involve repeated traction, chemicals, excessive heat, or extra hair. Endogenous or organic presentations of baldness include androgenetic alopecia, central centrifugal cicatricial alopecia (CCCA), discoid lupus erythematosus (DLE), and sarcoidosis.

A comprehensive algorithm to address hair thinning and loss within this cohort, one which encompasses these reasons, will also

be presented. Specific practical daily care, including commercial product options, will also be discussed. The goal is for dermatologists to gain an understanding of the natural presentation of black hair, the adverse consequences which can result from styling and organic conditions, and therapeutic options to combat both types of hair loss.

The Use of Bercaplermin 0.01% Gel in Refractory Foot Ulcers Secondary to Chronic Graft versus Host Disease

Tracey D. Brown-Maher^{1,2} Margo Cashin;² Barbara Moyst;² Alain Brassard;³

1. Private Practice, St. John's, NL; 2. Eastern Health, St. John's, NL; 3. University Dermatology Centre, Edmonton, AB

Goals and Objectives: Bercaplermin 0.01% gel (recombinant human platelet-derived growth factor) has been used to treat many types of chronic wounds, including diabetic foot ulcers, neuropathic ulcers, and scleroderma-type ulcers. Sclerodermoid graft versus host disease (GVHD) presents as atrophy and skin tightness with hyper- and hypopigmentation. There is increased risk of ulceration. Ulcers are quite difficult to heal, and often complicated by secondary infection due to chronic immunosuppression. We present a case of recalcitrant foot ulcers secondary to chronic sclerodermoid GVHD treated with Bercaplermin 0.01% gel.

Purpose: To treat recalcitrant foot ulcers secondary to sclerodermoid chronic GVHD in a 6 year-old girl. She developed chronic GVHD after a bone marrow transplant for severe combined immunodeficiency (performed at age 1). She failed multiple treatments including silver-based dressings and non-adhesive foams, monthly extracorporeal phototherapy treatments, and repeated courses of intravenous antibiotics.

Methods: Due to her recalcitrant ulcers and the sclerodermoid changes in her skin, we felt daily Bercaplermin gel would be a viable option. This was applied to her wounds and covered with Promogran, an oxidized cellulose and collagen-based dressing. The Bercaplermin gel was supplied by Johnson and Johnson Wound Management, a division of Ethicon, Inc.

Results: At two months, her wounds displayed healthy granulation tissue and were decreased in size. We hope that her wounds will continue to improve and eventually close with the use of Bercaplermin.

Discussion/Conclusion: The mechanism of action of bercaplermin gel includes stimulation of the inflammatory wound cascade, attraction of inflammatory cells which cleanse the wound, and the stimulation of proliferation of connective tissue and formation of granulation tissue. This may explain its efficacy in this case. The combination of Bercaplermin and Promogran may serve as an effective tool for treating other difficult chronic wounds and requires further study.

Challenging Wound Care Cases in a Multidisciplinary Wound Care Clinic

Tracey D. Brown-Maher,^{1,2} Margo Cashin,² Barbara Moyst,² David Jewer,² Arthur Rideout,² Donald Fitzpatrick,² Gregory Browne,² Craig Stone,²

1. Private Practice, St. John's, NL; 2. Eastern Health, St. John's, NL

Our multidisciplinary wound care clinic began in November 2006. It involves Dermatology and Surgery specialties (Vascular, Plastics and Orthopedics) and nurses trained in wound care. We are involved in cases referred from all over our province. In a little over one year we have seen multiple different types of ulcers, each with their own unique challenges.

The ulcer etiologies include pressure, venous, arterial, diabetic, post-surgical, trauma, graft versus host disease, and autoimmune. Most interesting cases included resistant venous ulcerations, foot ulcers secondary to sclerodermoid chronic graft versus host disease, "idiopathic" calciphylaxis, diabetic foot osteomyelitis caused by coagulase negative staphylococcus and radiation-induced foot ulcers (secondary to plantar wart treatment). The approach to these ulcers was tailored to the individual patient and situation, and included benzoyl peroxide lotion, bercaplermin, honey, hyperbaric treatment, and collagen/cellulose-based dressings. Interestingly, we saw infrequent wound contaminants/infections such as clostridium perfringens and stentrophomonas maltophilia. Complications included contact dermatitis and development of MRSA in new patients.

The most frustrating obstacles were treatment of resistant organisms, cost of dressings, adequacy of community care (including home IV therapy), and of course, patient compliance. Most patients were significantly improved or healed with treatment. Anecdotal feedback from patients, community health nurses, and physicians was extremely positive.

In-Vivo Evaluation of the Diameter (Lateral Size) of the Differential Polarization Signal Emerging from Human Skin

Gurbir Dhadwal, Lioudmila Tchvialeva, Harvey Lui, David Mclean, Tim K. Lee; Photomedicine Institute, Department of Dermatology and Skin Science, University of British Columbia and Vancouver Coastal Health Research Institute; and Cancer Control Research Program and Cancer Imaging Department, BC Cancer Agency.

Objectives: The goal of this study was to measure the diameter (lateral size) of the differential polarization signal emerging from human skin in order to evaluate the bulk optical parameters of normal human skin (NS) and seborrheic keratoses (SK).

Background: Unscattered or weakly scattered light maintains its original polarization stage, whereas multiple-scattered light is randomly polarized. If linear polarized light is used to illuminate the skin, the fraction of light retaining the original polarization is generated by surface reflection, weak superficial scattering and multiple scattering. Cross-polarization captures multiple-scattered light from deeper layers of tissue. The difference between the two signals is referred to as the differential polarization signal; it elimi-

nates the multiple-scattered light and can be used to determine the optical properties of the superficial skin layers. Previous studies conducting Monte-Carlo simulations have shown that the diameter of the differential polarization signal is of the order of a few transport mean free path-lengths (TMFP). Therefore, by measuring the diameter of the differential polarization signal we can assess in-vivo the bulk optical parameters of skin lesions, which maybe able to further infer the cell structure of the lesion.

Methods: Polarized red and blue diode laser light were used to illuminate in-vivo the NS and SK of human volunteers using diaphragms of differing diameters to alter the area from which scattered light was collected. Co-polarized and cross-polarized images were captured with 2 CCD cameras with input polarizers. The mean intensities over the images were then used to calculate the ratio of the differential polarization signal to the total light emerging from the open area. This scaling generates a fraction of linear polarized light (FOLP), a more convenient parameter for comparing among different subjects. The FOLP was plotted versus diaphragm size, allowing the diameter of emerging light spot to be evaluated; at diaphragm sizes larger than the spot diameter, the FOLP is expected to approach an asymptote.

Results: For NS as the size of the diaphragm for light collection was decreased the FOLP of backscattered red laser light increased; no significant difference was seen with blue laser light. For SK as the size of the diaphragm was decreased the FOLP for both backscattered red and blue laser light were increased. Using bulk optical parameters taken from the literature for normal skin, the expected light spot diameters were calculated and were found to be comparable with the measured diameters. The TFMP for SK was found to be longer than for normal skin.

Conclusions: The conducted evaluation of diameter of the emerging differential polarization signal concurs with calculations using reference data. For the first time in our knowledge the bulk optical parameters of SK were evaluated in-vivo. The long TFMP may be explained by the underlying pathology. A possible explanation is keratin cysts may provide a larger scattering anisotropy causing the increase in the TFMP. Through simple non-invasive measurements, the radial distribution of the FOLP can be used for in-vivo evaluation of the bulk optical parameters, and, hence, the cell structure of superficial skin lesions.

The Presence of Regression Should not be an Indication for Sentinel Lymph Node Biopsy in Thin Melanoma

Pierre-luc Dion,¹ Antoine Kibrité,² Éric Gagné,² Joël Claveau,²

1. CHUQ - L'Hôtel-Dieu de Québec, Saint-Nicolas, QC; 2. CHUQ - L'Hôtel-Dieu de Québec, Québec, QC

Breslow thickness and ulceration of the primary tumor are recognized predictors of nodal metastasis and survival. The prognostic significance of primary tumor regression on the other hand has been debated in the literature. Some authors argued that it represents an adverse prognostic factor since it leads to underestimate what would have been the "real" Breslow thickness in the absence of any regression.

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Between August 1996 and November 2007, 653 patients with melanoma (Breslow > 1,00 mm, Clark level IV/V or ulcerated) had a sentinel lymph node biopsy (SLNB) at our Melanoma Clinic. SLNB was also performed on 40 patients whose primary melanoma showed histological evidence of significant regression but did not meet the accepted criteria.

For our cohort of 653 patients, the mean age was 54,7 years old. The median Breslow thickness was 2,28 mm and 22.4% had one or more positive SLN. In the "regression-only" group, the mean age was 55,0 years old. Six patients had an in situ melanoma, one patient had a completely regressed lesion, and the median Breslow thickness in the 33 patients remaining was 0,60 mm. None of the "regression-only" patients had a positive SLN. Therefore, according to these results, we believe that regression should not be used as a single criterion to justify a SLNB in the absence of other recognized high risk predictors of SLN involvement (Breslow > 1,00 mm, Clark level IV/V or ulceration).

An Ultrastructural Study of 127 Patients with Fabry's Disease

Jeff C. Donovan^{1,2}, Ronald E. Gordon,² Robert G. Phelps;²

1. University of Toronto, Toronto, ON; 2. Mount Sinai School of Medicine, New York, NY, USA

Introduction: Fabry's disease is an X-linked recessive disease caused by α -galactosidase deficiency and leads to the accumulation of glycosphingolipid in lysosomes of various tissues. Enzyme replacement therapy, with drugs such as Fabrazyme® or Replegal®, may be slow disease progression, in part, through clearance of glycosphingolipids from the vascular endothelium. Remarkably, clearance of inclusions from the dermal capillary endothelium mirrors clearance from several other organ systems and thus skin biopsy can serve as a good surrogate to monitor overall disease progression.

Most clinical experience with enzyme replacement therapy has been derived from studies involving male patients. An important unresolved issue is the timing of treatment initiation for female heterozygotes. Whether the abundance and distribution of glycosphingolipid inclusions on skin biopsy differ in female heterozygotes and whether the efficacy of enzyme replacement therapy differs in this group of patients is unknown.

Methods: Using light microscopy and electron microscopy, we compared the frequency and distribution of glycosphingolipid inclusions in skin biopsies between 51 male patients and 76 affected female heterozygotes. The average age was 39 years and 17 patients were under the age of 18.

Results: Inclusions were present in multiple cell types by both light and electron microscopy. Compared to female carriers, males had a greater frequency of inclusions seen by electron microscopy in superficial endothelial cells (43 % vs 9 %, $p < 0.001$), deep endothelial cells (57 % vs. 25 %, $p = 0.01$), perineural fibrocytes (61 % vs 30 %, $p = 0.0006$) and vascular smooth muscle (49 % vs 32 %, $p = 0.048$).

Conclusion: Electron microscopy remains a valuable resource for assessing patients and carriers with Fabry's disease. The reduced level of endothelial inclusions seen in biopsies from female carriers warrants further study to determine whether this impacts the efficacy of enzyme replacement therapy.

Development of an *in-vitro* Model of Skin Immune Function

Jeff Donovan^{1,2}, Tariq Dawoud¹, Gwendalyn Randolph¹, Miriam Merad¹

1. Department of Gene and Cell Medicine, Icahn Research Institute, Mount Sinai School of Medicine, NY, USA; 2. Division of Dermatology, University of Toronto, Toronto, ON

Background: The development of representative *in-vitro* models to study dermatological diseases must account for the complex interplay between multiple cell-types within the epidermis and dermis. Currently bioengineered skin equivalents are based on an epidermis derived solely from keratinocytes. These models are typically devoid of other cell types, especially antigen presenting cells. Useful *in-vitro* surrogate models to study immunologically-based skin disease, such as contact hypersensitivity, cutaneous infection, drug reactions and vaccines will ultimately require the incorporation of these components. We set out to develop an *in-vitro* surrogate for future use in studies of skin immune function.

Methods: A technique was developed to seed the dermis from a commercially available skin equivalent with endothelial cells derived from human umbilical vein endothelial cells. After 4 days of culture, blood donor-derived peripheral blood mononuclear cells were added to the endothelial layer, and the skin equivalent was cultured for an additional 7 days. Thereafter, the histology of the skin equivalent was examined by H&E staining. The presence of MHC class II-positive (antigen presenting cells) within the epidermis and dermis, and specific markers of epidermal Langerhans cells such as CD1a, were examined by immunofluorescence microscopy.

Results: Histology of the skin equivalents confirmed the presence of a well-differentiated stratified epidermis above the dermis, along with an endothelial layer beneath the dermis. Immunofluorescence staining indicated the presence of MHC class II positive cells within the dermis as well as within the basal and suprabasal layers of the epidermis. CD1a positive cells were also identified in the epidermis.

Conclusion: We established a human skin equivalent model that contained antigen presenting cells. Studies are ongoing to further characterize this model and to evaluate the *in-vitro* responsiveness of the skin equivalent to cytokine or antigenic stimulation.

Comparative Study of IQ and Finn Chambers Test Methodologies in Detecting Ten Common Standard Allergens That Cause Allergic Contact Dermatitis

Joseph Doumit;¹ Melanie Pratt;²

1. The Ottawa Hospital, Ottawa, ON; 2. Division of Dermatology, University of Ottawa, Ottawa, ON

Background: Patch testing is routinely used in contact dermatitis clinics since it is the gold standard for the evaluation of potential allergic contact dermatitis.

Objectives: The present study was undertaken to evaluate possible differences in reactivity between the Finn Chamber and IQ patch testing methodologies.

Methods: Between the period of December 16th, 2005 and December 15th, 2006, 214 patients were patch tested simultaneously with the Finn Chamber and IQ patch tests. Ten standard allergens set by the North American Contact Dermatitis Group (NACDG) were utilized for both techniques. They include Formaldehyde 1.0% aq, Ethylenediamine dihydrochloride 1.0% pet, Bisphenol A epoxy resin 1.0% pet, Quaternium 15 - 2.0% pet, 4-tert-butylphenol formaldehyde resin 1.0% pet, Mercapto mix 1.0% pet, Black rubber mix pet 0.6%, Potassium dichromate 0.25% pet, Myroxylon Pereirae 25.0% pet and Nickel sulfate 2.5% pet.

Results: From the 405 positive reactions obtained, 206 (50.9%) were positive with the Finn Chambers, 199 (49.1%) with IQ tests and 358 (88.4%) with both methods. The Finn Chamber methodology was more efficient at detecting Formaldehyde, Quaternium 15 and Nickel sulfate; missing 12.9%, 2.6% and 2.94% respectively of all positive reactions. In contrast, the IQ methodology was somewhat better in detecting Potassium dichromate, missing 14.3% of positive reactions.

Conclusions: The Finn Chamber performed better at detecting Formaldehyde, Quaternium 15 and Nickel sulfate whereas the IQ was better in the detection of Potassium dichromate.

Non-Invasive Computer Aided Method in Measuring Skin Ulcers

Joseph Doumit;¹ Tad Pierscianowski;² Jonathan Couturier;³

1. Faculty of Medicine, University of Ottawa, Ottawa, ON; 2. Division of Dermatology, University of Ottawa, Ottawa, ON; 3. Faculty of Engineering, University of Ottawa, Ottawa, ON, Ontario

Background: Ulcer measurements are an important factor in determining the healing progress of an ulcer and in evaluating the efficiency of different treatment modalities.

Objective: To develop a user friendly software tool that calculates a precise and reliable measurement of the surface area of a skin ulcer from a digital image. The software must not have any restrictions on the location or angle of the ulcer image.

Methods: Preliminary tests of the software were completed with images of objects of known surface area. The software was proven to be accurate with an error margin of less than 4.3%. Twelve leg

ulcers from 9 patients were then measured using graphical grids and the surface area was calculated in mm². The same ulcers were photographed using a digital camera. Each ulcer was captured at different angle, zoom and brightness. The images were then uploaded to the computer software for measurement analysis.

Results: The difference in the surface area between the traditional and image processing technique was 12.7%. The coefficient of variation was of 6.3% which shows that both methods agree with a minute discrepancy.

Conclusion: The digital photographic method was shown to be a user friendly and an accurate method to calculate the surface area of leg ulcers.

Longer Term Experience with Infliximab in Hidradenitis Suppurativa and Pyoderma Gangrenosum: a Case Series of 9 Patients

Aaron M. Drucker;¹ Warren J. Winkelman;² Scott Walsh;³ Neil H. Shear;³

1. Queen's University School of Medicine, Kingston, ON; 2. Medical Department, Schering-Plough Canada, Toronto, ON; 3. Division of Dermatology, University of Toronto, Toronto, ON

Introduction: Infliximab, a tumour necrosis factor-alpha (TNF- α) antagonist, approved for use in plaque psoriasis, may also be effective for long-term control of other inflammatory dermatoses, including pyoderma gangrenosum (PG) and hidradenitis suppurativa (HS)(1,2).

Methods: A retrospective chart review of 9 patients treated with infliximab: 5 with PG and 4 with HS, refractory to all previous therapies.

Results and Conclusions: One patient's HS was quiescent for 2 years after receiving only 2 infusions, and another had quiescent disease after 4 infusions. Two of three female HS patients had concomitant polycystic ovary syndrome (3), with both patients demonstrating HS disease quiescence after receiving relatively few infusions. In PG, complete healing was seen in 2 patients with 2 other patients continuing to heal. One other PG patient had shown initial improvement but had a flare after his 4th infusion. Additionally, three of 4 PG patients on high-dose prednisone (≥ 20 mg/day) before starting infliximab were either weaned off prednisone completely or weaned down to a low dose (≤ 2 mg/day) by 6 months after the start of treatment, indicating that infliximab may have steroid sparing effects in PG. Only mild adverse events were experienced by three patients during infusions, none of which necessitated discontinuation of therapy. Although infliximab 5 mg/kg appears to be safe and effective in some cases of recalcitrant PG and HS, formal studies are necessary to determine optimal dose and infusion schedule.

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Non-Classical Congenital Adrenal Hyperplasia: Presentations to the Dermatologist

Maha Dutil, University of Toronto, Toronto, ON

Non-classical congenital adrenal hyperplasia, also known as late-onset congenital adrenal hyperplasia, is much more common than the classical form, with a frequency ratio as high as 1 per 27-100 in certain ethnic groups. It is under-diagnosed, and in women is often misdiagnosed as PCOS because of the similarity of presentations.

In young women, late-onset congenital adrenal hyperplasia may present with:

- acne alone (including the severe nodular form, refractory to therapy with oral antibiotics, and isotretinoin)
- androgenetic alopecia in the absence of other hyperandrogenic symptoms
- hirsutism

In boys, late-onset congenital adrenal hyperplasia may present with:

- early beard growth
- early onset androgenetic alopecia
- severe acne refractory to oral antibiotics and isotretinoin.

This presentation will briefly review three cases of late-onset congenital adrenal hyperplasia (2 females and 1 male) presenting to a dermatologist. It will review important features in the history, physical exam, and the key laboratory investigations required to make this diagnosis. The importance of gene testing and the risk of spontaneous abortions and classic congenital adrenal hyperplasia in progeny will also be discussed. The presentation will include a review of treatment options.

Mediterranean Pearls 2008

Benjamin K. Fisher, Hertzliya Medical Centre, Hertzliya-Pituach, Israel

Mediterranea Pearls 2008: Several Unusual and challenging cases seen in Israel in 2008 will be shown. Audience participation is greatly encouraged.

Ultraviolet Light Mediated Induction of Systemic Lupus Erythematosus-Like Disease in NOD Mice: A Model of Environmentally Induced Autoimmunity

Mehran Ghoreishi, Jan P. Dutz; Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC

The role of environmental precipitants in autoimmunity such as systemic lupus erythematosus (SLE) remains unclear. Here we demonstrate that ultraviolet light B (UVB) with or without topical

application of synthetic Toll like receptor 7 ligand (imiquimod) induces SLE like disease in auto-immune prone non-obese diabetic (NOD).. Repeated weekly exposures of mice to UVB alone (dose) or combined with topical imiquimod (dose) induced auto-antibodies against chromatin, dsDNA, sm-RNA or RNP detectable by direct immunofluorescence of HEP cells and antibody against desmoglein 3 (Dsg3) by ELISA. Apoptotic cells were significantly increased in skin following UV irradiation. Following UV irradiation, IFN α inducible gene MxA expression was detectable in skin of treated mice with or without TLR7 agonist. Systemic immune activation was detected following combination (UVB and imiquimod) therapy as evidenced by IL-6 production in serum. This treatment resulted in glomerulonephritis measured by PAS staining of glomeruli and proteinuria. Immune complex depositions were detectable in dermo-epidermal junction, follicular epithelial cells and in glomeruli of kidney in 20% of experimental mice. Combined treatment induced B cells from PBMC showed up-regulation of TLR-7 in an IgD bearing population. Pristane induces auto-antibody induction in Balb/C mice 12-20 weeks after ip injection. High mobility group box 1 (HMGB1) a chromatin protein has been implicated in immune complex mediated autoimmune pathogenesis. In our studies HMGB1 was expressed in extracellular compartments of skin after treatment with UVB and imiquimod but not in normal control mice. These studies demonstrate UV induction of systemic autoimmunity and suggest synergistic roles of UV induced local inflammation and TLR7 engagement in which HMGB1 may contribute.

Pachyonychia Congenita with Laryngeal Obstruction

Richard M. Haber; Derek Drummond; University of Calgary, Calgary, AB

Pachyonychia congenita (PC) is a rare autosomal dominantly inherited genodermatosis. Clinical features in addition to the thickened nails include palmoplantar hyperkeratosis, follicular keratoses and leukokeratosis of the oral mucosa. Rarely leukokeratosis of the larynx can occur in this condition, resulting in laryngeal obstruction which is potentially life-threatening.

I wish to report on a two year old girl with pachyonychia congenita who developed stridor and respiratory distress due to leukokeratosis of her larynx. This required treatment with a carbon dioxide laser.

To my knowledge, there are only four other reports of laryngeal obstruction in PC in the literature, although hoarseness suggesting laryngeal involvement has been reported more frequently.

As patients with PC often present to dermatologists, they need to be aware that laryngeal involvement can occur in PC and can manifest as a potentially life-threatening complication of this disease.

Using the US Experience with Physician Assistants to Shape Their Role in Canadian Healthcare

Sameh Hanna; Private Practice, Lancaster, PA, USA

Physician Assistants (PAs) have been a growing component of the health-care workforce in the United States since 1965. They are

represented in all medical fields including Dermatology. Outside of the military context, the entry of PA's into the Canadian health-care field is a relatively recent development. Canadian dermatologists, should consider the American experience with PAs to help manage and optimize their integration into Canadian dermatologic care.

In reviewing the medical and PA literature (and from firsthand experience with PAs), many benefits are noted. A PA may alleviate patient access problems to dermatologic care on the short term, may be an additional revenue stream for the physician and can free a physician to care for more complex cases while "routine" entities are cared for by the PA. However these benefits are accompanied by certain concerns. What is an appropriate level of training and supervision? Who will set curricula for Physician Assistant specialist training? If specialist education of PAs is to be "on-the-job", who will monitor its adequacy and effectiveness? What are appropriate levels of autonomy and supervision and who will establish, regulate and enforce them? How should PA's services be reimbursed? Perhaps most importantly, are we treating our patients fairly using non-physician mid-level providers as a means of extending health-care access?

Once PAs enter the health-care work-force, they will be a permanent fixture. Though the PA societies are adamant that what distinguishes PAs from other mid-level providers is their generalist training and strict reliance on Physician supervision, as they progress in their careers and the public grows more familiar with the concept, there may be a tendency to seek greater autonomy. Therefore, we must carefully consider all of these issues proactively so we are ready to direct the role PAs will have in delivering Dermatologic care in Canada.

A Randomized Prospective Double-Blind Placebo-Controlled Clinical Study Assessing the Efficacy of Clobetasol Propionate 0.05% and Tacrolimus 0.1% Ointments in Treating Children Vitiligo

Nhung T. Ho; Elena Pope; Miriam Weinstein; Saul Greenberg; Christine Webster; Derek Stephens; Bernice R. Krafchik; University of Toronto, Toronto, ON

Background: Both clobetasol propionate 0.05% (CP 0.05%) and tacrolimus 0.1 % (T 0.1%) ointments have been shown to be efficacious and safe in treating vitiligo. It is unknown which one is more efficacious and safer in the paediatric population.

Objective: To assess and to compare the efficacy and safety of these two topical therapies.

Methods: In this prospective double-blind placebo-controlled study, 100/106 children (2-16 year old), treated for a 6 months duration, were randomized to one of the three arms: 1) CP 0.05% ointment for a 2 months on, 2 months off (CP 0.05% substituted with placebo) cycle (n=33), 2) T 0.1% ointment (n=34) or 3) placebo (n=33) continuously for 6 months; with further stratification to "face" and "non face" groups. Successful repigmentation, defined as >50 % improvement, was evaluated by comparing photographs taken at baseline, 2, 4 and 6 months.

Results: In the facial group, 58% of the CP 0.05% group responded successfully compared with 58% of the T 0.1% group (p=0.57).

In the non-facial group, 39% of the CP 0.05% group responded successfully versus 23% of the T 0.1% group (p=0.30). There were significant differences in response between the CP 0.05% and the T 0.1% groups vs placebo (p <0.0001) and (p=0.0004) respectively. 24% (7/29) of the placebo-treated facial group had some repigmentation (5 with <50% repigmentation, 2 with >50%), representing 2.4% spontaneous repigmentation. The most common pattern of repigmentation was diffuse in the CP 0.05% group; diffuse and mixed in the T 0.1% group. Some transient erythema was noted and no atrophy.

Conclusions: Both CP 0.05% and T 0.1% ointments are efficacious in repigmenting pediatric patients with both facial and non facial vitiligo. The facial lesions responded faster. There were no significant adverse events noted.

Two Concurrent Cases of Occupational Contact Dermatitis to Phenol-Formaldehyde Resin Adhesives in the Wood Manufacturing Industry: The Use of Open Patch Testing to Raw Materials.

Brandon G. Howell¹; Sandy Skotnicki-Grant²

1. University of Toronto Dermatology Resident, Toronto, ON; 2. University of Toronto, Toronto, ON

Phenol formaldehyde (phenolic) resins are poly-condensation products of phenols and aldehydes. Phenol-formaldehyde resins have many industrial applications including moisture resistant adhesives and glues used in the construction industry. We present two cases of contact dermatitis to phenolic resin adhesives in the manufacture of exterior handcrafted wooden doors and veneered windows. The door-maker developed chronic hand dermatitis. The window-maker, working with heated phenolic resin adhesives, developed a more extensive eruption on the arms and face. As with epoxy resin systems, patch testing with the actual resin to which the worker is exposed is important. No single substance or standard set of allergens reliably detects allergy to the wide variety of phenolic resins. On account of daily direct skin exposure to these resins, patch testing with the raw materials was performed using an open un-occluded method without dilution. Interestingly, common allergens were discovered for these divergent clinical presentations. Furthermore, it was determined that the door-maker was only allergic to exterior door phenol resin adhesives. He could continue to work with the materials used for interior doors. Open testing to raw materials enabled this conclusion, and allowed him to stay at his workplace. If raw material testing had not been done, this would not have been discovered.

Richner-Hanhart Syndrome : Report of a Case

Valérie Joncas;¹ Marc-andré Rhéaume;¹ Nicole Fallaha;² Grant A Mitchell;² Afshin Hatami;²

1. Centre Hospitalier de l'Université de Montréal, Montréal, QC; 2. CHU Ste-Justine, Montréal, QC

Background: Tyrosinemia type II (Richner-Hanhart syndrome) is an autosomal recessive disease caused by a deficiency of the hepatic enzyme tyrosine aminotransferase (TAT) leading to an accumulation of tyrosine in all tissues resulting in characteristic oculo-cutaneous manifestations and variable mental retardation.

Case: A 19 month-old Lebanese boy of consanguineous parents presented with a 2-month history of painful localized thickening of the palms and soles.

The patient was followed by ophthalmology from the age of 8 months for bilateral dendritiform corneal lesions. A diagnosis of herpetic keratitis was made and treatment with intravenous acyclovir was initiated. Recurrence of the ocular symptoms necessitated two more hospitalisations before the age of one.

Physical examination at the dermatology clinic revealed an irritable child with painful punctate hyperkeratoses of his finger pads, thenar eminences and plantar surfaces.

Viral cultures and serology for HSV IgM-IgG were negative.

The diagnosis of hypertyrosinemia type II (Richner-Hanhart) was suspected and confirmed with a blood tyrosine level of 1546 µmol/l (normal 40-85 µmol/l).

The child was started on a diet low in tyrosine and phenylalanine following evaluations by medical genetics and a nutritionist. Dietary restriction resulted in rapid resolution of skin and eye manifestations.

Discussion: Richner-Hanhart syndrome, also known as tyrosinemia type II, is caused by a deficiency of the cytosolic fraction of the hepatic enzyme tyrosine amino-transferase. The chromosomal location of the TAT gene has been located to chromosome 16.

Skin manifestations consist of painful focal hyperkeratosis distributed on palms and soles. Spontaneous remission of ocular pseudo-dendrites in this syndrome has been reported elsewhere, and as seen in our case, can give the false impression of a clinical response of herpetic keratitis to treatment.

Early dietary intervention is a critical step that should be started upon confirmation of the diagnosis.

Persistent Facial Psoriasiform Dermatitis: A Newly Described Dermatoses Discovered Through Modern Live Patient Teaching Rounds

Sunil Kalia;¹ Richard I. Crawford;^{1,2} Brian T. Kunimoto;¹ Jerry Shapiro;¹ Jason K. Rivers;¹ Harvey Lui;¹

1. Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC; 2. Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC

Introduction: A novel pattern of comparable cases has arisen from our departmental live patient presentation rounds at the University of British Columbia. These cases had the following constellation of features: i) facial preference; ii) persistent, discrete, scattered, salmon-coloured, thin, and round to oval papules with fine white scale; iii) histology resembling psoriasis or seborrheic dermatitis; iv) resistance to a range of anti-inflammatory therapies.

Methods: Between 1996 to 2008, eleven patients were identified from our database amongst those who had been referred to our weekly university case rounds with an undiagnosed refractory facial dermatosis. Of these eleven patients, two were excluded because histopathology was not compatible, and one patient declined to have their clinical data included in this series.

Results: The mean age of the eight patients was 38.4 years (range: 21-70 years); there were 4 males and 4 females. In six of the eight patients the eruption only appeared on the face. All cases revealed scattered well demarcated salmon-coloured, round to oval, 0.5-1.0 centimeter thin papules with fine white scale. Seven biopsies taken from six patients all showed psoriasiform epidermal hyperplasia with prominent parakeratosis, follicular plugging, and a purely lymphocytic superficial perivascular infiltrate without evidence of an interface dermatitis. Topical therapy with corticosteroids ranging from hydrocortisone to clobetasol (n=5), calcipotriol (n=2), tacrolimus (n=5), ketoconazole (n=3), metronidazole (n=2) were all unsuccessful as were intralesional triamcinolone (n=2), isotretinoin (n=1), minocycline (n=2), and UVB phototherapy (n=3).

Conclusion: This clinical pattern has not been previously reported in the literature to our knowledge. The condition has been named persistent facial psoriasiform dermatitis to characterize the natural history of this facial cutaneous eruption that shows psoriasiform and lupoid clinical features and histology resembling psoriasis or seborrheic dermatitis. The maintenance of teaching rounds along with their formal documentation can provide a means for detecting and characterizing previously unidentified and perhaps less common pathological conditions periodically encountered by experienced clinicians.

Comparative Efficacy and Safety Evaluation of Benzoyl Peroxide 5%/Clindamycin 1% Topical Gel to a Benzoyl Peroxide 2.5% Combination Treatment System

Leon Kircik, Indiana University, Indianapolis, IN, USA and Physicians Skin Care, PLLC, Louisville, KY, USA

Appearance is an important aspect of quality of life. This is particularly true for acne patients of all ages who have become susceptible

to media and advertising campaigns promising clear skin with “dermatologist-approved” products available without a prescription. Impatience for results often renders them vulnerable to abandoning prescribed anti-acne regimens in favor of those endorsed by celebrities or media-spokespeople.

The fixed combination of topical benzoyl peroxide (BPO) 5%/clindamycin 1% in a moisturizing gel has demonstrated efficacy and tolerability in the treatment of acne. The premixed combination containing dimethicone and glycerin offers advantages in both efficacy and tolerability over monotherapy with either agent alone. Recently, millions of consumers have begun to use a non-prescription, multiphase skin care system based on BPO 2.5% to combat their acne lesions. Some patients perceive this system to be an alternative to a physician visit or prescription product. Additionally, the thought is that a “kit” or prepackaged system would enhance patient compliance or potentially work faster.

This 12-week, multicenter, investigator-blinded, randomized parallel group pilot study compared the efficacy and safety of once-daily fixed combination BPO/clindamycin gel to the twice daily use of the BPO 2.5% system in 64 subjects with moderate to severe acne. While both treatments improved acne lesions, the median percentage change from baseline in inflammatory lesions was statistically significant at -81% in the combination gel group and -64% in the BPO 2.5% group ($p=0.0195$) at week 12. Also at week 12, 45% of subjects in the fixed combination therapy group and 18% of subjects in the BPO 2.5% group showed investigator global assessment reductions of ≥ 2 categories ($p=0.0285$).

Patient compliance was also a key factor analyzed in this study. As early as week 4, 93% of subjects in the BPO/clindamycin treatment group indicated that it was ‘very easy’ or ‘easy’ to comply with the treatment compared to 48% of subjects treated with the BPO 2.5% system. No adverse events were reported for the combination gel therapy while 4 instances of burning, erythema and peeling were reported with the BPO 2.5% group.

Colchicine In Dermatology: Off-Label use in Fifty Patients

John N. Kraft; Scott Walsh; Division of Dermatology, University of Toronto, Toronto, ON

Background/Objectives: Colchicine is a water-soluble alkaloid that interrupts mitosis through microtubular toxicity and has anti-inflammatory effects. It has been used in dermatology, without formal indication, for a variety of cutaneous diseases, especially neutrophilic dermatoses. Case reports have shown variable success of colchicine in treating other diseases including erythema nodosum, leukocytoclastic vasculitis, recurrent aphthous stomatitis, and even chronic urticaria.

Methods: We conducted a retrospective chart review of 50 patients treated with off-label uses of colchicine in a university hospital ambulatory clinic. Response to colchicine was graded as good, moderate, or poor. A good clinical response was defined by a response or remission in greater than 90% of patients treated. A moderate clinical response was reserved for diseases in which there

was response or remission in greater than 50% of patients treated or remission when used as an adjunct agent with another therapy. A poor clinical response referred to diseases in which less than 50% of patients responded to colchicine.

Results: Good clinical responses to colchicine were observed in bullous lupus, chronic erythema nodosum, dermal hypersensitivity syndrome (lymphoeosinophilic infiltrate of skin), leukocytoclastic vasculitis, minor aphthous stomatitis, relapsing polychondritis, and urticarial vasculitis. Moderate clinical responses were seen in bullous pemphigoid, dermatitis herpetiformis, epidermolysis bullosa acquisita, linear IgA disease, and mucosal membrane pemphigoid. Finally, poor clinical responses to colchicine were seen with chronic idiopathic urticaria and lichen planus. Overall, the drug was well-tolerated with diarrhea being the only dose-limiting side-effect.

Conclusions: The mechanisms of action of colchicine make it well-suited to treat a variety of dermatological conditions. It was well-tolerated in our patients and is generally safer in moderate doses and less expensive than most immunosuppressive agents. Dermatologists should consider colchicine as a valuable agent in their armamentarium, especially for treating skin diseases with neutrophilic infiltrates.

The Psoriasis and Arthritis Screening Questionnaire (PASQ): A Sensitive and Specific Tool to Diagnose Psoriatic Arthritis Patients with High Correlation to the CASPAR Criteria

Ian D. Landells¹; Majed Khraishi¹; Catherine Heale²; Gerry Mugford²; Belinda Grouchy¹

1. Nexus Clinical Research, St. John's, NL; 2. Memorial University of Newfoundland, St. John's, NL

Introduction: Psoriatic arthritis (PsA) affects 10-35% of patients with psoriasis and is associated with increased morbidity and mortality. In 2006 the Classification Criteria for PsA (CASPAR) was introduced for diagnosing PSA, however, we designed the psoriasis and arthritis screening questionnaire (PASQ) to facilitate in identifying patients at high risk of developing PsA. The objective of this research is to examine the PASQ sensitivity to CASPAR diagnostic criteria.

Methods/Materials: An evaluation of PASQ, containing ten questions and a diagram for patients to label joint swelling/pain in a rheumatology and dermatology clinic based population of psoriasis/ PsA patients. Scores were obtained for the PASQ and diagram, and cumulatively, to a maximum score of 15. CASPAR criteria were assessed through chart review and for the utility of the PASQ in detecting subjects who meet CASPAR criteria ROC curves using MedCalc[®] were obtained. Descriptive statistics were obtained by SPSS.

Results and Conclusions: Data collected on 58 patients (49% male) citing a history of psoriasis and arthritis. Mean age: 52 ± 11.19 , duration of skin disease: $20.18 \text{ years} \pm 13.5$. 7 subjects did not meet CASPAR criteria. Analysis of PASQ scores with the ROC curve [AUC = 0.878, 95% C.I.: 0.766 to 0.949, $p=0.0001$] indicated a total score of 6

yielded 78.43% sensitivity, 85.7% specificity. Analysis of cumulative scores [AUC = 0.916, 95% C.I: 0.813 to 0.972 p=0.0001] yielded a cut-off score of 9, with 86.27% sensitivity, 85.71% specificity. Preliminary data suggests that the PASQ, with high sensitivity, is effective at detecting patients who meet CASPAR criteria. Continuing studies are ongoing involving the utilization of PASQ in identifying psoriasis patients that have high risk of developing PsA.

Etanercept Treatment in Children and Adolescents with Plaque Psoriasis

Richard G. Langley,¹ Amy S. Paller,² Elaine C. Sigfried,³ Alice B. Gottlieb,⁴ David Pariser,⁵ Ian Landells,⁶ Adelaide A. Hebert,⁷ Lawrence F. Eichenfield,⁸ Vaishali Patel,⁹ Kara Creamer,⁹ Angelika Jahreis⁹

1. Dalhousie University, QEII Health Sciences Centre, Halifax, NS; 2. Children's Memorial Hospital, Northwestern Medical School, Chicago, IL, USA; 3. Kids Dermatology, St. Louis, MO, USA; 4. Tufts - New England Medical Center, Boston, MA, USA; 5. Eastern Virginia Medical School and Virginia Clinical Research, Inc., Norfolk, VA, USA; 6. Nexus Clinical Research, St. John's, NL; 7. University of Texas Dermatology Clinical Research Center, Houston, TX, USA; 8. Rady Children's Hospital and University of California, San Diego, CA, USA; 9. Amgen Inc., Thousand Oaks, CA, USA

Introduction: Treating PsO in children is challenging.

Methods: In this 48-wk study, 211 children (4 to 17 yrs) with PsO involving $\geq 10\%$ body surface area and PASI score ≥ 12 were randomly assigned 1:1 in a 12-wk double-blind (DB), placebo (Pbo)-controlled treatment period to once-weekly subcutaneous Pbo or ETN 0.8 mg/kg (<50 mg), followed by 24 wks of open-label (OL) ETN, then a 12-wk randomized DB withdrawal-retreatment period. Pts who did not achieve PASI 50 at wk 24 or PASI 75 at wk 36 could add topical standard of care therapy. The primary endpoint was PASI 75 response at wk 12.

Results: Baseline demographics and disease characteristics were similar across treatment arms. At wk 12, 57% of ETN pts achieved PASI 75, compared with 11% of those who received Pbo ($P<0.001$); proportions of pts who achieved PASI 50, PASI 90, and PGA clear-almost clear were also significantly greater in the ETN arm than the Pbo arm. At wk 24, percentages of pts who achieved PASI 75/PGA clear-almost clear were 62%/56% for the original Pbo arm and 69%/57% for the original ETN arm. PASI 75 response was maintained through week 36; 56% (original Pbo arm) and 53% (original ETN arm) had PGA clear-almost clear. Exposure adjusted rates of non-infectious adverse events (431/100 pt-yr Pbo, 288/100 pt-yr ETN) and infections (308/100 pt-yr Pbo and 229/100 pt-yr ETN), were comparable between the 2 groups; most events were mild or moderate. Upper respiratory tract infection, headache, and nasopharyngitis were the most common events. During the withdrawal period, no pt experienced PsO rebound or change of PsO morphology.

Conclusions: In this study, ETN was well-tolerated and provided significant and sustained improvement in disease severity in children and adolescents with moderate to severe plaque PsO.

Successful Treatment of Complex Aphthosis with Colchicine and Dapsone

Carrie B. Lynde,¹ Alison J. Bruce,² Roy S. Rogers III,³

1. Faculty of Medicine, University of Toronto, Toronto, ON; 2. Division of Clinical Dermatology, Mayo Clinic, Rochester, MN, USA; 3. Division of Clinical Dermatology and Division of Laboratory Dermatology, Mayo Clinic, Rochester, MN, USA

Introduction: We investigated the effectiveness of colchicine and dapsone in patients with complex aphthosis-recurrent oral and genital aphthous ulcers or severe, almost constant, multiple oral aphthae in the absence of Behçet syndrome.

Methods: We conducted a retrospective review of medical records of patients with complex aphthosis evaluated and treated at Mayo Clinic, a tertiary care medical clinic, between 1998 and 2007. Fifty-five patients with complex aphthosis were treated according to the clinic's therapeutic ladder, starting with colchicine and adding dapsone to treatment of patients who did not have a substantial response (more than 75% improvement) to colchicine or who discontinued colchicine because of adverse effects.

Results: Overall, most patients (80%) had a substantial response to therapy and had no serious adverse effects. Fifty patients received colchicine as monotherapy, with 60% (30/50) achieving therapeutic success and no need for additional treatment. Fourteen patients received a combination therapy of colchicine and dapsone; of these patients, 71% (10/14) had treatment success. Five patients received dapsone as monotherapy and 4 (80%) had a substantial response.

Conclusions: In this retrospective case series, colchicine and dapsone were effective, safe therapies for treatment of complex aphthosis. The clinic's experience demonstrates that colchicine and dapsone, 2 long-standing drugs that are well-established medications for gout and leprosy, respectively, and for other dermatologic disorders, should be considered efficacious in the treatment of complex aphthosis.

How Dermatologists Can Transition to a Cosmetic Procedure Based Practice

Stuart Maddin, Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC

Introduction: Dermatologists who place a greater emphasis on performing cosmetic procedures fail to recognize the intrinsic value of medical dermatology in successfully developing a cosmetic practice. A practice with medical dermatology at its foundation will have earned the confidence of their existing patient base, as well as confirm that the physicians are established clinicians who possess a comprehensive level of knowledge and skills relating to the skin. Consequently, their recommendations will be perceived as those based on a more well-rounded perspective and not regarded as solely for the purpose of financial gain.

Methods: The strategies that will be outline are based on personal experiences gained through more than twenty years in clinically and academically based practices. This presentation will emphasize the basic essential elements that dermatologists should employ in

transitioning from a medical to a cosmetic practice, which is quite apart from the focused training and suitable office space that is required to engage in this competitive sub-specialty. Determining whether one should purchase or lease equipment and how to train staff will be discussed. Key areas that warrant focused consideration include: where will your patients come from; which procedure should you concentrate on; how can you ethically promote your services and “how to grow” your practice.

Conclusion: The primary objective of this discussion will be to provide clinicians with essential information in formulating a business plan, as well as explore if the necessary elements are in place prior to incorporating cosmetic procedures into their existing medical practice. In doing so, it is hoped that the exercise will improve the synergistic benefits derived from such a combined practice.

Contact Sensitization Therapy with Diphenacyprone in the Treatment of Cutaneous Metastases of Melanoma

Andrei I. Metelitsa; Thomas G. Salopek, Division of Dermatology and Cutaneous Sciences, University of Alberta, Edmonton, AB

Introduction: Approximately three percent of patients with melanoma will develop recurrence of their disease manifesting as satellitosis or in-transit metastasis. Although multiple treatments have been tried, none resulted in consistent disease control. Contact sensitization therapy refers to the treatment of cutaneous disease by induction of allergic contact dermatitis in the area of application. Diphenacyprone (DPC) is a commonly used antigen in the treatment of alopecia areata and warts. There have been three anecdotal reports documenting the successful use of DPC in the treatment of melanoma. The proposed mechanism of action involves a delayed hypersensitivity reaction induced by DPC that presumably incites lymphocyte-mediated tumor destruction.

Method: Patients with dermal cutaneous metastasis were recruited into the study. They were initially sensitized to DPC 2% ointment under a Finn chamber occlusion for 48 hours. Those who demonstrated a reaction were seen in follow-up and titrated to a minimal concentration of DPC required to induce an immune response. On a weekly basis, increasing concentrations of the DPC ointment was applied (from 0.01% to 0.1%) until each patient developed a mild, pruritic, scaly patch at the site of application. Thereafter, the patients self-applied DPC ointment under occlusion for 24 hours weekly at the optimal concentration that induced this reaction.

Results: All patients who developed a reaction to DPC upon initial sensitization developed a variable eczematous reaction to the site of application of DPC. In addition to the inflammatory response seen clinically, there was readily apparent shrinkage if not complete obliteration of their dermal cutaneous metastases. On histology, sites of sensitization revealed a brisk, severe inflammatory insect bite-like reaction with numerous chronic inflammatory cells, plasma cells, eosinophils and melanophages. There was no evidence of viable melanoma cells.

Conclusions: Topical DPC may prove to be a simple, cost-effective, efficacious treatment for cutaneous metastasis of melanoma, as demonstrated by clinical and histological destruction of the

melanoma metastasis. The treatment was well-tolerated with no untoward adverse responses noted.

Acrogeria?

Loukia-maria Mitsos;¹ Regean Drouin;² Dominique Hanna;³

1. CHUS, Montreal, QC; 2. CHUS, Department of Genetics, Sherbrooke University, QC, Canada, Sherbrooke, QC; 3. CHUS, Division of Dermatology, Department of Medicine, Sherbrooke University, QC, Canada, Sherbrooke, QC

Introduction: Acrogeria is a rare congenital disorder characterized by cutaneous atrophy and loss of subcutaneous fat most prominently over the acral skin giving rise to the prematurely aged appearance.

Methods: We report the case of a 5 year old girl, who presented the following clinical manifestations: micrognathia, alopecia, prominent scalp veins, short stature, growth delay and thin and wrinkled skin. Besides these morphological abnormalities, she had an atrial septal defect. She is the first child of the family with a younger healthy brother. The gestation and labor were unremarkable.

Results: Conventional cytogenetic studies and FISH (fluorescence in situ hybridization) using subtelomeric probes were performed on the lymphocyte culture and no chromosomal abnormalities were identified. The patient, by Q-FISH analysis, showed a dramatically reduced telomere length in comparison to her sibling and even her parents. The Telomere Restriction Fragment (TRF) analysis, which assessed the average telomere length of the whole genome, confirmed the short telomere length observed by the Q-FISH. The sequencing of LMNA (lamin A) gene did not reveal any mutations, therefore excluding the diagnosis of progeria.

Conclusion: Acrogeria is a very rare premature aging syndrome. We are presenting the first case of telomere dysfunction in acrogeria. Molecular studies of genes implicated in telomere biology can help to further delineate this syndrome.

A New Psoriatic Skin Model for Dermopharmaceutical Applications

R. Pouliot^{1,2}, J. Jean^{1,2}, G. Bernard^{2,3}, M. Auger³, J. Soucy⁴

1. Faculté de Pharmacie, Université Laval, Québec; 2. Laboratoire d'Organogénèse Expérimentale (LOEX), Hôpital du St-Sacrement, Québec; 3. Département de Chimie, Université Laval, Québec; 4. Département de dermatologie, Hôpital de l'Enfant-Jésus, Québec

Introduction: Psoriasis is a skin disease that affects 2% of the world population¹. It is well known that psoriatic skin has a highly altered stratum corneum (SC) and, as a consequence, impaired permeability function. Lipids present in skin play a crucial role in the maintenance of the skin barrier. Indeed, modifications in the composition or organization of intercellular lipids modify the permeability properties of the skin. The SC of psoriatic and healthy skin substitutes were obtained by tissue engineering techniques to compare the lipid organization and protein conformation. The aim of these studies is to develop a robust in vitro model of psoriasis that could be used as a valuable tool in basic research and drug discovery.

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Methods: Psoriatic and healthy skin substitutes were produced using the auto-assembly method. The fibroblasts were cultured in presence of ascorbic acid at a concentration of 50 µg/ml. These cells formed easy to handle sheets which were superimposed and incubated for seven days to form a new dermal layer. Keratinocytes were seeded on the dermal layer to form a new epidermal layer. Skin substitute biopsies were taken at 21 days after being raised to the air-liquid interface and they were examined by histology and immunohistochemistry. Of particular interest for studying SC lipids are the bands between 2800 and 3000 cm⁻¹ in FTIR spectra. These bands are due to C-H stretching vibrations primarily associated with the lipid alkyl chains.

Results: Results show that the cutaneous substitutes produced through tissue engineering are macroscopically similar to psoriatic skin. We noticed whiter and thicker substitutes when using psoriatic cells, which corresponds to an accumulation of dead cells on the surface due to the acceleration of cellular division observed in psoriasis. Also, the expression of transglutaminase in these substitutes appears earlier than in those produced with healthy cells. Mason's trichrome staining of slices of psoriatic substitutes has showed a thickening of the stratum corneum (hyperkeratosis) as well as a loss of the granular layer (agranulosis). Our FTIR results suggest that the stratum corneum of psoriatic skin substitutes is less organized and more permeable than that of normal human skin. These results are in good agreement with in vivo observations. Variable results were obtained for uninvolved psoriatic SC when compared to normal SC. For one cell line, FTIR results were the same for controls and uninvolved psoriatic substitutes. In contrast, for the other psoriatic cell lines, higher frequencies were obtained. It therefore seems that the properties of uninvolved psoriatic skin may vary with seriousness of the disease.

Conclusion: Psoriatic skin is known to be more permeable than normal human skin. Our results suggest that the stratum corneum of our psoriatic skin substitutes is less organized and more permeable than the one of normal human skin. The observations made from psoriatic skin substitutes produced by tissue engineering concur with the observations made from psoriatic lesions found on patients. Further studies are needed to correlate these results with other cell lines from psoriatic donors. This model could become an effective and innovative dermopharmaceutical tool for the screening of new treatments.

Alterations of the Oral Mucosa in Children

Marcia Ramos-e-Silva, Brazil

The oral mucosa can be the site of various modifications and diseases, among them are normal anatomical variations, development alterations and congenital defects. Color may greatly vary and thus white, red, violaceous or hyperpigmented lesions may be observed. Ulcers, as aphthae, bullous diseases, as pemphigus and pemphigoid, infectious diseases, and traumatic lesions, as well as diseases of other organs and systems (nutritional, metabolic, hormonal, hematological and psychosomatic diseases) can have manifestations inside the oral cavity. Also the mouth can be the location of many types of tumors, both benign and malignant.

Children are special targets to some these problems, which will be discussed with emphasis to the diagnosis and treatment.

Intralesional Corticosteroids (ILS) - Review and Recommendations

Robert N. Richards; Private Practice, Toronto, ON

Introduction: Dermatologists have used ILS for 50 years. Detailed instructions regarding technique and dosage are absent in standard references.

Methods: Analysis standard texts and Medline, 35 questionnaires from dermatologists (nearly 1000 practice years), 40 years of personal experience including intermittent observation of 40 office dermatologists.

Conclusions: The usual procedure is triamcinolone acetonide 10 mg/ml diluted with saline or plain lidocaine to 2.5-3.3mg/ml with total of 3 ccs (7.5-10 mg) every 3 to 4 weeks. (Some use higher concentrations). No systemic reactions (except allergy) ever reported. Keloids receive 10-40 mg every 3 to 4 weeks. Plastics often use higher doses but only rare reports of adrenal suppression. Sparse early studies show that triamcinolone acetonide up to 20mg did not produce significant adrenal suppression. All evidence indicates we can safely increase our ILS from 3ccs to 5 or 6ccs, i.e. total of 15mg (small people) or 20mg (big people) every 3 to 4 weeks; i.e. less visits and better results. Concerns? - monitor serum cortisol.

Retinal artery occlusion was reported with older products, in hemangiomas and intranasally (ENT). No problems reported with triamcinolone when used for psoriasis, eczema and alopecia et al near eyes.

Several dermatologists and texts indicated no ILS use for dermatitis. The original 1960s studies demonstrated excellent results for localized dermatitis and we agree. Atrophy dose related. Rare with 2.5mg/ml. Infections unusual. Most near bony prominences or tendon sheaths. ILS is safe, economical, and effective.

Ethyl Chloride Spray for Sensory Relief for Botox Injections of the Hand and Feet

Robert N. Richards; North York General Hospital, University of Toronto, Toronto, ON

We have found ethyl chloride spray to be more effective and rapid in relieving the discomfort of palmar and plantar Botox injections than other modalities; such as nerve blocks, vibration, and various forms of icing. Patients that have experienced other procedures inform us that they prefer the ethyl chloride spray.

The patient lies on the examination table and the ice pack which has been previously held by them (in the waiting room and / or examination room) for 1 to 4 minutes is removed.

We use Gebauer's ethyl chloride medium stream spray held 3 to 9 inches (8 to 24cm) away from the injection site and sprayed for 1 to 4 seconds until the skin just begins to blanch. We perform 2 to 6 injections before proceeding to the next site. Care is taken to

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withdraw the needle from the spray path or else the Botox solution freezes. The total hand procedure takes 2 to 4 minutes and there are no after effects from the ethyl chloride.

We are presently studying to see if we can further reduce sensations with Gebauer's ethyl chloride mist spray by combining ethyl chloride spray with topical anaesthetics such as Benzocaine gel, EMLA, or Maxilene.

Psoriatic Arthritis: Establishing a Cohort of Patients with Psoriasis

Cheryl F. Rosen; Vinod Chandran; Sutharshim Shanmugarajah; Fawnda Pellett; Sergio Toloza; Catherine Schentag; Dafna Gladman, Toronto Western Hospital, University of Toronto, Toronto, ON

A cohort of patients with psoriasis has been established to study the factors associated with the development of psoriatic arthritis (PsA) in these patients. Since January 2006, consenting patients diagnosed with psoriasis without arthritis by dermatologists are recruited from dermatology offices and phototherapy centres. Patients are evaluated by a rheumatologist to exclude PsA using questionnaires, physical examination, laboratory and radiographic evaluation, if required. People with psoriasis without PsA are seen yearly, or sooner if they develop symptoms of inflammatory articular disease. To date, 247 patients with psoriasis have been assessed. 219 (134 males) were diagnosed with psoriasis without PsA and enrolled for prospective follow-up. 28 patients (11.3%) had PsA at initial rheumatologic assessment and were excluded. In patients with psoriasis alone, the mean age at onset of psoriasis was 29 years, and the mean disease duration was 17 years. 40.6% (89) reported family histories of psoriasis, 1.8% (4) PsA, 3.7% (8) inflammatory bowel disease. 82% (179) had psoriasis vulgaris, 12% (26) had guttate psoriasis and 3% (6) had flexural psoriasis. 50% (110) of patients had psoriatic nail dystrophy. 93% (203) of the patients had received phototherapy, 20% (43) had received systemic therapy (methotrexate:12, cyclosporine:5, retinoids:20, sulfasalazine:1, mycophenolate mofetil:1, steroids:1, anti-TNF agents:6, alefacept:8, efalizumab:3). 33% (72) had a concurrent illness (45:hypertension, 7:ischemic heart disease, 9:diabetes, 9:cancer). Of note, 5.5% of people with psoriasis developed PsA within the first year of follow up. However, if people who were lost to followup are included in the analysis and are assumed to not have developed PsA, the incidence of PsA developing in people with psoriasis is 4%. Patients will continue to be followed annually.

Blepharoplasty as an Integral Part of Dermatologic Surgery Practice

Mariusz J. Sapijaszko; Division of Dermatology, University of Alberta, Edmonton, AB

Blepharoplasty continues to be a very popular and sought after aesthetic procedure. Both patients and physicians realize the importance of peri-ocular anatomy and aesthetics for optimal patients' well being. Eyes and the surrounding structures are a focal

point in facial aesthetics and their importance cannot be overemphasized.

Recently, more and more dermatologists are trained in blepharoplasty and perform this procedure with or without adjunctive therapies such as Botox®, fillers or laser technologies. Dermatologists who are surgically trained are ideal physicians to perform blepharoplasty as the signs and symptoms that lead patients to seek this procedure are frequently related to skin ageing.

Excessive upper and/or lower eyelid skin in association with laxity of orbital septum and related orbital fat protrusion lead to the classical "tired" look that our patients seek to avoid. Proper pre-operative assessment including examination of skin quality, thickness and elasticity are as important as the assessment of orbital septum and fat pockets. As such, dermatologists who are surgically trained can appreciate both surface and textural quality of peri-ocular skin as well as the underlying structures.

Frequently, blepharoplasty can be combined with Botox® or filler injections as well as laser phototherapies. Either percutaneous or transconjunctival approach can be combined with pre-operative Botox® injections as well as intra-operative Er:YAG or CO2 laser therapy. Again, these adjunctive therapies are well known to dermatologists who have uniquely played a role in their development.

The presentation will focus on unique abilities of surgically trained Canadian dermatologists in performing blepharoplasties in combination with other adjunctive modalities.

Nipple Surgery - Techniques and Results

Mariusz J. Sapijaszko; Division of Dermatology, University of Alberta, Edmonton, AB

Nipple aesthetics are a significant concern to both men and women. These include, among others, nipple size asymmetry, enlarged nipples in men and inverted nipples on women. Traditionally, nipple surgery has been a domain of plastic surgeons but recently dermatologists have been asked to help patients with this rather common concern. I am presenting examples of nipple surgeries performed in my office for both men and women.

Example one - 56 year old women presented with a long-standing history of inverted right nipple. Her left nipple was normal and the routine mammography of both breasts was unremarkable. She underwent subcision therapy as well as pursestring sutures to secure newly subcised and adjusted nipple.

Example two - 24 year old man presented with prominent protruding nipples bilaterally following prior piercing. Bilateral nipple surgery including subtle debulking and flap closure resulted in excellent aesthetic result.

Nipple inversion in women and nipple protrusion in men are significant aesthetic concerns. Although most of the corrective surgeries are performed by plastic surgeons, more and more dermatologic surgeons are asked to assist in this common problem. Several techniques are available to address individual anatomic variations. The details of these techniques will be presented with focus on the most practical and common methods available.

Patch Test Negative Contact Dermatitis

Denis Sasseville; Division of Dermatology, McGill University Health Centre, Montreal, QC

Patch testing is the gold standard tool to diagnose allergic contact dermatitis. It remains, however, a crude bioassay that does not reproduce daily conditions of exposure. According to Dr. Robert Rietschel, a positivity rate between 30% and 60% reflects appropriate use of a patch test clinic. But what about those patients who have negative results and why do they fail to react?

The causes of false negative reactions can be divided into two categories: True negative and false negative reactions. True negatives are seen when patients do not have contact dermatitis or suffer from non-allergic contact dermatitis.

False negative reactions occur when patients with allergic contact dermatitis fail to react when patch tested. The causes are numerous and include missed allergens, technical failure, patient-related failure, physician-related failure and compound allergy.

The most common cause of false negative reactions is failure to test the patient's allergens. This problem can be overcome by testing with an extended standard series, with supplemental series, and with the patients' own cosmetics and workplace products in adequate vehicles and appropriate dilutions.

Technical failure results from insufficient penetration of allergens because of inadequate occlusion from the support material, too short application time, too low a concentration or inappropriate selection of a vehicle that fails to release the allergen. Patient-related failure occurs because of non-compliance with the testing procedure, and immunosuppression. The most common cause of physician-related failure is the omission of late readings after 48 hours. Other causes include failure to perform early readings (15 to 90 minutes) in cases of contact urticaria, or to do photopatch testing in cases of suspected photocontact allergy. Compound allergy is a poorly understood phenomenon in which a formulated product produces a positive patch test reaction while its individual ingredients are negative.

The lecture will review all of the causes of negative patch tests and propose solutions to avoid the dreaded false negative reactions that lead to repeated episodes of unrecognized allergic contact dermatitis.

Lentigo Maligna and Micrographic Surgery with "Collerette" Procedure : 30 Cases

Jean-françois Sei; Véronique Chaussade; Ute Zimmermann; Arnold Tchakerian; Thierry Clerici; Brigitte Franc; Philippe Saiag, Hôpital Ambroise Paré, Boulogne, France

Introduction: The recurrence rate (RR) of lentigo maligna (LM) at 5 years is 20 % when using the generally accepted 5 mm margin of resection. With Mohs micrographic surgery, the RR is 3 % . We present a technique derived from the "fixed-tissue" Mohs surgical technique.

Methods: 30 LM were treated in 29 patients between December 1999 and May 2007. Removal of the LM was first made by full thickness excision with a 3 mm margin of normal surrounding skin. Conventional microscopy was performed to exclude dermal invasion. A 2 mm strip ("collerette") of normal looking skin around the edge of the wound was next removed. This strip was inked clockwise then formaldehyde-impregnated and embedded in paraffin. The outer border of the entire strip was systematically and entirely screened by standard microscopy with vertical sectioning. Additional surgical excisions were then performed as needed until negative margins were obtained.

Results: 20 women and 10 men, mean age 73, were treated by this technique. All LM were on the face. There were 23 primary tumors and 7 recurring tumors. The mean tumor size was 21mm X 16 mm. Primary closure was done whenever possible (15 cases). 10 cases required skin grafting. 5 cases healed by secondary intention. 23 cases required only one surgical procedure, 6 cases had two procedures and 1 case had 3 procedures. Only one recurrence occurred after a median follow up of 36 months,, treated with the same technique

Conclusion: This margin-control technique is simple. The recurrence rate appears clearly lower than by standard excision.

Incontinentia Pigmenti: A Retrospective Study of 30 Cases at the Centre Hospitalier Universitaire Ste. Justine

Danya Sereda¹, Jacques Michaud², Danielle Marcoux³

1. Division of Dermatology, Centre Hospitalier de l'Université de Montréal, Montreal, QC ; 2. Division of Genetics, 3. Division of Dermatology, Centre Hospitalier Universitaire Sainte-Justine

Introduction: Incontinentia pigmenti (IP) is a rare, X-linked dominant disease affecting multiple systems including the skin, central nervous system, eyes, and teeth. It is almost always lethal in males and variably expressed in females. The diagnosis of IP is usually made based on characteristic clinical manifestations and biopsy findings. Donnai and Landy's clinical criteria stratify patients suspected of having IP into 2 groups depending on the presence or absence of IP in a first-degree family member. Definitive diagnosis is achieved by identifying mutations in the *NEMO* gene, with 80% of patients showing a deletion of exons 4-10 (*NEMOΔ4-10*).

Methods: Patients with a diagnosis of IP followed at the CHUS were identified by searching pathology and archive databases. Charts of patients with IP were reviewed and information recorded regarding dermatological and systemic manifestations. Both main hospital charts and medical genetics files were consulted to determine which patients had undergone genetic testing for the *NEMOΔ4-10* mutation.

Results: Thirty charts of patients with IP were reviewed. Twenty-nine patients were female and 1 was male. Dates of birth ranged from 1976 to 2007. All patients had dermatological findings. Of the 25 patients with a documented neurological evaluation, 10 (40%) had neurological anomalies including convulsions, encephalopathy, psychomotor retardation, and learning disabilities. Twenty-five patients had documented ophthalmological examinations, with

28% showing anomalies including retinal vasculopathy, strabismus, and retinal detachment. Seventy percent of evaluated patients had dental anomalies, 58% scalp alopecia, and 30% nail anomalies. Among patients without a documented first-degree family history, all had at least one major Donnai and Landy criteria, and over half had one or more minor criteria. All patients with an affected first-degree family member had at least one major Donnai and Landy criteria. Eight patients (all female) underwent genetic testing for the *NEMOΔ4-10* mutation. Seven tested positive, and 1 negative. Of the seven with a positive test, 6 had neurological anomalies, 6 had dental anomalies, and 1 had an ophthalmological abnormality. The patient who tested negative had only skin lesions and skin biopsy consistent with IP, and no other documented abnormalities. The only male in our series did not undergo genetic testing, and had only skin lesions and biopsy consistent with IP.

Conclusions: In our series, 40% of patients had one or more neurological abnormalities. This is slightly higher than the approximate 30% quoted in the literature, perhaps because we included patients who developed learning disabilities. Twenty-eight percent of our patients had ophthalmological anomalies, comparable to the 20-35% seen in previous series. Dental anomalies were seen in 70% of our patients, within the reported range of 59-85%. Not enough patients in our series underwent testing for the *NEMOΔ4-10* mutation to correlate this genotype with a particular phenotype or determine the sensitivity or specificity of the Donnai and Landy criteria. Our findings, however, highlight the necessity of a multi-disciplinary approach to care in these patients, since while skin lesions usually ultimately resolve with little sequelae, neurological, ophthalmological, and dental manifestations of IP can be serious and permanent if not treated early. Additionally, further study of the long-term neurological, ophthalmological, and dental outcomes for patients with IP is warranted.

Keratinocytes' Terminal Differentiation Signaling Pathway Involves Dual Leucine Zipper Kinase

Carolyne Simard-Bisson; Hubert Robitaille; Richard Blouin; Lucie Germain, LOEX/Centre de recherche du Centre hospitalier affilié universitaire de Québec and Department of Surgery, Laval University, Québec, QC

A well orchestrated differentiation of the keratinocytes is essential for the renewal and differentiation of the epidermis. This complex process requires intracellular pathways involving signaling molecules that are not completely known. Among these molecules, we have identified Dual Leucine Zipper Kinase (DLK) as a good candidate to command the keratinocyte differentiation since its expression is restricted to the granular layer where living keratinocytes terminally differentiate into dead corneocytes.

Objectives: Study the impact of DLK on the terminal differentiation of keratinocytes as well as its interaction with proteins well known for their involvement in this process such as the transglutaminase 1 (TG1) and the caspase 14. The first molecule is considered as responsible of the assembly of the cornified envelope and the second is thought to signal keratinocytes' death.

Methods: The effect of DLK overexpression using viral vectors on the differentiation level of cultured human keratinocytes was deter-

mined. The interaction of DLK with TG1 or caspase 14 was studied by immunoprecipitation followed by western blot as well as immunolocalization by transmission electronic microscopy. To study the effect of DLK on transglutaminase's activity, cultured keratinocytes overexpressing DLK were incubated with a fluorescent substrate of TG1 and observed by fluorescence microscopy.

Results: Our observations show that DLK's overexpression in cultured keratinocytes stimulates the apparition of a differentiated phenotype, increases the activity of TG1 and the cornification process as well as the activity of ERK and JNK which are important molecules for the signaling and regulation of this process.

Conclusion: These results indicate that DLK is sufficient to induce keratinocyte's terminal differentiation and provide tools to better characterize the molecular signaling involved in the formation of stratum corneum.

Self-healing Juvenile Mucinosis

Pascale St-Amour; Jean Bernard; Isabelle Auger; Éric Gagné; CHUQ, Québec, QC

Introduction: Mucinosis represent a spectrum of rare diseases characterized primarily by cutaneous deposition of mucine. One of the forms of mucinosis described in literature is called Self-Healing Juvenile Mucinosis (SHJMC). Few cases have been reported thus far but the disease presents a particular clinical pattern.

Method: We herein describe the case of an eleven year old boy who first presented a history of an acute cutaneous eruption. The child was otherwise completely asymptomatic. Upon physical examination we noted periorbital edema, multiple firm yellowish papules on the neck and forehead and two firm non-tender nodules, the first on the right elbow and the second on the first PIP joint of the 3rd right finger. Clinical laboratory examination was normal. A biopsy of a lesion on the neck showed a superficial mucine deposit compatible with a SHJMC.

Discussion: SHJMC was described for the first time in 1973. Thereafter fourteen cases have been described in literature. A review of these cases allows us to document the primordial characteristics of this entity: young age at onset, particular distribution of cutaneous lesions, presence of nodules, rapid onset and self-limiting course.

Differential diagnosis are multiple and include other forms of mucinosis, rheumatoid arthritis and proliferative fasciitis

Mucine deposits in mid and deep reticular dermis, arborizing thin-walled vessels and prominent plump spindle-shaped fibroblasts seen upon papule biopsy and involvement of subcutaneous tissue with sparing of dermis upon nodule biopsy have been described thus far.

Thus it is essential to correlate clinical findings with a thorough laboratory workup and biopsy to correctly identify this self-limiting disease requiring no treatment.

Squamous Cell Carcinoma of the Skin-A Broad Range of Risks

Thomas Stasko; The Vanderbilt Clinic, Nashville, TN, USA

Like melanoma, the incidence of Squamous Cell Carcinoma of the skin (SCCS) has been rising. If, as some propose, actinic keratoses (AK) are regarded as SCCS, it is the most common of all human malignancies. Even if AK are excluded, over 250,000 new cases of SCCS develop each year in the United States. Because SCCS is excluded from most tumor reporting systems the exact number is unknown. In a similar manner, the number of deaths from SCCS is also uncertain, but probably exceeds 2000 each year. The risk of metastasis of SCCS has been estimated to be 5% over 5 years. A broad spectrum of disease spans the gaps between early simple sun-induced SCCS, destructive, deeply invasive tumors and metastatic disease. The challenge to the clinician is recognition of the degree of risk of progression in each patient so appropriate therapeutic plans and follow-up schemes may be developed.

In almost all situations, sun exposure and fair skin are major risk factors for the development of SCCS; however, it is important to recognize other factors which may predispose an individual to aggressive SCCS. These factors include genetic syndromes such as xeroderma pigmentosum, chronic immunosuppression due to organ transplantation or other diseases, lymphoma or leukemia, excessive PUVA treatments, radiation dermatitis and chronically injured skin. Tumors in these situations often require more aggressive treatment and closer follow up. Because these individuals may also develop large numbers of SCCS, alternative therapies including field therapies and systemic chemoprophylaxis may need to be considered. Tumor characteristics have also been identified which are associated increased risks of recurrence, metastasis and death. In one reported series all SCCS-related deaths were noted to have at least one of the following characteristics: size > 4 cm, perineural invasion or deep invasion beyond subcutaneous structures. For these tumors additional investigations to evaluate the extent of the tumor and possible metastases is often warranted. In addition to complete removal of the tumor, adjunct therapy such as radiation or chemotherapy may be appropriate.

After the diagnosis of SCCS, the clinician must carefully evaluate each patient and each lesion to determine the level of risk and develop appropriate intervention.

Gene Expression Signatures of the Lesional Skin in Patients with Vitiligo Vulgaris

Ming-wan Su¹, Yanhua Liang², Wency Ip¹, Aie Xu³, Harvey Lui¹, Shen Yang², Xiejun Zhang², Youwen Zhou^{1,2}

1. Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC; 2. Institute of Dermatology, Anhui Medical University, Hefei, Anhui, China; 3. Department of Dermatology, Third People's Hospital, Hangzhou, Zhejiang, China

Background: The molecular pathogenesis of vitiligo vulgaris is unclear. Understanding the genomic transcription differences

between lesional and normal skin in patients with vitiligo may uncover new clues on vitiligo pathogenesis.

Objectives: The goal is to identify genes that are abnormally transcribed in lesional skin compared with perilesional skin in patients with vitiligo vulgaris.

Materials and Methods: With approval by the Clinical Ethics Board of University of British Columbia, twenty five patients with vitiligo vulgaris were recruited for the study. Each patient donated two full-thickness skin biopsies, one from the perilesional normal skin, and the other from the de-pigmented area. Each biopsy was divided into two portions. One portion was used for RNA extraction. The other was used for confirming the status of melanocytes and for cellular localization of gene transcription changes. The total cellular RNA was isolated and used to probe high-density DNA microarrays representing the entire human transcriptome. The expression differences between lesional and normal skin of each patient were obtained by interrogating the data set using GeneSpring data mining software, and verified using quantitative PCR, in situ RNA hybridization and immunofluorescence.

Results: Specific and reproducible gene transcription changes were revealed between vitiligo lesional skin and normal perilesional skin. Two genes (VU-1 and VU-2), which were known to be expressed by lymphoid cells, were moderately up-regulated in the lesional skin. In contrast, five genes (VD-1 to VD-5) were markedly down-regulated. Four down regulated genes (VD-1 to VD-4) are known lineage markers of melanocytes. The fifth down regulated gene (VD-5), however, was previously unknown to be expressed by the skin cells. In situ hybridization and immunofluorescence analyses revealed that the VD-5 gene product was present in the membrane of keratinocytes of normal skin. However, the keratinocytes of vitiligo lesional skin were defective in the production of this protein. Sequence analysis revealed no promoter mutation in this gene.

Conclusions: Novel genomic transcription defects were uncovered in the lesional skin of patients with vitiligo vulgaris. The observed down regulation of a gene in the lesional keratinocytes suggests a changed (and perhaps hostile) microenvironment for the melanocytes. Further study is underway to further test the significance of VD-5 gene and the epidermal microenvironment in the pathogenesis of vitiligo.

New Non-Approved Indication of TNF- α Inhibitors in Inflammatory Skin Diseases

Zohair Tomji; Memorial University, St. John's, NL

Tumor necrosis factor-alpha (TNF- α) is a proinflammatory cytokine that plays an immunomodulatory role in the variety of systemic and dermatologic diseases. Currently, three anti-TNF- α drugs are available in North America - infliximab (approved for the treatment of rheumatoid arthritis), etanercept (approved for the treatment of rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and psoriasis), and adalimumab (approved for the treatment of rheumatoid arthritis, psoriasis, and psoriatic arthritis). A growing number of published reports suggest

that anti-TNF- α therapies may be effective in the treatment of numerous inflammatory skin diseases outside their currently approved indications.

Pediatric Mycosis Fungoides, Case Report and Literature Review on Current Treatments

Anh Tran;¹ Kim Tran;² Catherine Ruddy;¹ Elena Pope;³

1. University of Ottawa, Ottawa, ON; 2. McMaster University, Hamilton, ON; 3. University of Toronto, Toronto, ON

Up-to-date, the literature on Pediatric Mycosis Fungoides is still limited. We present a case of a 12 year old Caucasian male, who were adopted. He had a 2 years history of hypochromatic, scaly macules on his trunk, neck, arms and upper legs. With the occasional itch, he was otherwise asymptomatic. The differential diagnosis included pityriasis alba, eczema, pityriasis rosea, tinea versicolor, sarcoid or hypopigmented mycosis fungoides. The skin scraping for KOH was negative. His complete blood work, liver function tests, chest x-ray and abdominal ultrasound were normal. Antibodies of HTLV-I or HTLV-II were not detected. Microscopic examinations of two biopsies, on his right flank and back, were diagnostic of Patch-type Mycosis Fungoides. He was started on narrow band UVB three times per week in incremental doses. Review of literature on current treatments of Pediatric Mycosis Fungoides is included.

A Review of Benzophenone-3 in Sunscreens

Anh Tran;¹ Cheryl Rosen;²

1. University of Ottawa, Ottawa, ON; 2. University of Toronto, Toronto, ON

Concerns have been raised about human percutaneous absorption, urinary excretion and systemic effects following topical application of benzophenone-3. A systematic literature review was done to evaluate all published studies in order to address this issue. Medline, PubMed and Google Scholar were each searched three times from October 2007 to January 2008. All papers and abstracts were reviewed and further articles were obtained by examining the references of published papers. Over 700 papers and abstracts were found in the search, and approximately 35 were found to be relevant. In vitro studies used diffusion cells to examine benzophenone-3 absorption. In vivo studies were performed in animals and humans. Benzophenone-3 was measured in epidermal samples obtained by tape stripping, and in blood, urine and feces. Excretion of benzophenone-3 was measured in urine collected over different time periods in different studies, ranging from 10 hours to 10 days. The urinary excretion of benzophenone-3 was reported to be between 0.4 to 8.7% of the applied amount. Microscopic examination of tissues was used to detect effects of benzophenone-3 on internal organs of rats. Differences and similarities between studies, and weaknesses and strengths of each have been evaluated. This review confirmed that percutaneous absorption of benzophenone-3 does occur, and that it is excreted mainly in the urine. It is important to note that topical application of benzophenone-3 did not result in accumulation of benzophenone-3 in human tissues and that no toxic effects in humans have been demonstrated.

A National Survey to Evaluate the Impact of Psoriasis Among Canadian Patients

Norman Wasel;¹ Yves Poulin;² Robin Andrew;³ Daphne Chan;³ Elisa Fraqueli;³ Kim Papp;⁴

1. Stratica Medical and University of Alberta, Edmonton, AB; 2. Private Practice, Quebec, QC; 3. Ortho Biotech Canada, Toronto, ON; 4. Probit Medical Research, Waterloo, ON

Introduction: Psoriasis is a chronic inflammatory disease associated with many co-morbidities. There are no population based studies on psoriasis in Canada. The objectives of this national survey were to better understand the severity and impact of psoriasis on the lives of Canadian patients.

Methods: A 30-minute on-line survey was conducted using a consumer panel. The target sample size was 400. Eligible subjects reported a diagnosis of psoriasis by a physician and were currently or over the past five years suffering from moderate, severe, or very severe plaque psoriasis. Additionally, subjects had to:

- Have a minimum BSA of 3% using the palm method, or
- Have psoriasis on a sensitive area of the body (eg. face, scalp, genitals, palms or feet), or
- Be currently taking prescription oral or injectable medication or undergoing phototherapy

Results and Conclusions: In December 2007, e-mail invitations were sent to 3,845 panellists. A total of 514 met criteria. Mean age was 49.7 with a male to female ratio of 1:2. As much as 65% reported having moderate, severe or very severe psoriasis and 61% had a BSA > 3, while 24% had a BSA >10%. Nearly all subjects (96%) had psoriasis affecting a sensitive area. Most common symptoms were scaling (69%), skin redness (61%) and itchiness or sensation of burning (51%). Results showed that 18% of moderate, severe or very severe subjects were taking either prescription oral, injectable or phototherapy and of those subjects having a BSA >10, 47%. Co-morbidities were highly prevalent, with 75% reporting a least one. Overweight/obesity (32%), hyperlipidemia (26%), and high blood pressure (30%) were the most prevalent comorbidities. More than half felt that psoriasis made them self-conscious, inconvenienced, embarrassed and frustrated. Psoriasis is a major burden in the lives of Canadian patients with many being under-treated.

Management of the Pediatric Patient with Nevoid Basal Cell Carcinoma Syndrome: A Case Report and Review of the Literature

Monika Winnicki;¹ Catherine McCuaig;²

1. University of Montreal, Montreal, QC; 2. University of Montreal, CHU Sainte-Justine, Montreal, QC

Introduction: Gorlin Syndrome, or Nevoid Basal Cell Carcinoma Syndrome (NBCCS), is an autosomal dominant genetic syndrome caused by a mutation in the PTCH gene on chromosome 9. Most common features include multiple basal cell carcinomas (BCCs), odontogenic keratocysts, palmoplantar pits, calcification of the falx cerebri, and macrocephaly. The primary dermatologic feature is the

appearance of multiple basal cell carcinomas at a young age. The management of these often numerous basal cell carcinomas in the pediatric patient can pose a significant challenge.

Methods: The medical chart and clinical photographs of a patient with Gorlin Syndrome were reviewed. A discussion of the management of the young patient with Gorlin Syndrome is presented with a focus on the treatment options for multiple basal cell carcinomas in the pediatric population.

Results and Discussion: A three year old female patient with a history of developmental delay, macrocephaly, hypertelorism and agenesis of the corpus callosum presented with multiple tan to brown pedunculated papules on the buttock, thighs, feet, axilla and face. Biopsy of these lesions showed multiple BCCs. Genetic testing revealed a frame shift mutation in the PTCH gene and confirmed the diagnosis of Gorlin Syndrome. Hundreds of basal cell carcinomas were treated successfully with electrodesiccation and curettage under general anaesthesia. Topical 5-fluorouracil and imiquimod were used to treat lesions in localized areas.

Management of the cutaneous sequelae of NBCCS begins with the prevention of BCCs by early diagnosis and strict adherence to photoprotective practices. Chemoprevention of BCCs with oral retinoid has also been employed. Treatment of BCCs has included electrodesiccation and curettage, surgery, cryosurgery, Moh's micrographic surgery, topical agents including 5-fluorouracil and imiquimod, intralesional interferon, paclitaxel and more recently trichloroacetic acid peel, photodynamic therapy and CO2 laser. In pediatric patients with Gorlin Syndrome, goals are to minimize the number of painful procedures and scarring.

Cooperation of Tumor Suppressor ING1b and SWI/SNF Chromatin Remodeling Complex in Nucleotide Excision Repair

Ronald Pak Cheung Wong, Leon Hanyang Lin, Gang Li; Department of Dermatology and Skin Science, Jack Bell Research Centre, Vancouver Coastal Health Research Institute, University of British Columbia, Vancouver, BC

UV radiation (UVR) is the major environment risk factor for the development of skin cancers including melanoma. It induces DNA lesions such as cyclobutane pyrimidine dimers (CPDs) and pyrimidine (6-4) pyrimidone photoproducts (6-4PPs) which are repaired by the nucleotide excision repair (NER) pathway. Efficient NER pathway is important to protect cells from mutation and genomic instability and thus to tumorigenesis of skin cancers. DNA is packed in a compact structure called chromatin which is inhibitory to all DNA transactions including NER. Therefore, it is proposed that chromatin remodeling precedes NER and is necessary to provide favorable environment for recruitment of repair factors to UV lesions. However, the role of chromatin remodeling in NER is not fully understood. We have previously showed that tumor suppressor ING1b enhances NER through histone H4 acetylation and chromatin relaxation. It is also required for the localization of DNA lesion recognition, XPA, to CPD lesions. We recently found that ING1b interacts with SNF5, core subunit of the ATP-dependent chromatin remodeling complex, by immunoprecipitation in melanoma cell line MMRU and also in 293 cells. Unlike ING1b, SNF5 binding to chromatin did not change upon

UV radiation. To further study the cooperation of SWI/SNF complex with ING1b in NER, we established stable cell line with SNF5 knock-down using SNF5 short-hairpin RNA in 293 cells. We found that UV-induced chromatin relaxation was abrogated in cells with SNF5 knockdown using Micrococcal nuclease digestion assay. This data shows that ING1b may cooperate with SWI/SNF complex as chromatin remodeling factors in NER. It sheds light on the molecular mechanisms of how UV-damaged DNA is repaired which eventually enables us to design effective strategies for skin cancer prevention.

Microarray Analysis of Lichen Planopilaris and Pseudopelade of Brocq Suggest They are Distinct Entities

Mei Yu, Megan Isaac-Renton, Elizabeth K. Ross, Magda Martinka, Jerry Shapiro, Kevin J. McElwee; Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC

Pseudopelade of Brocq (PPB) and lichen planopilaris (LPP) are the most common primary cicatricial (scarring) alopecias encountered. Because these diagnoses share so many signs and symptoms, their distinct nosological identities have often been questioned. The purpose of this study was to identify how similar PPB and LPP are by gene expression profiling. Alopecia affected, and clinically normal haired, scalp tissue biopsies were obtained from 8 untreated patients diagnosed clinically and histologically with PPB or LPP. Microarray analysis, using a 21K expanded sequence verified cDNA set was performed. Differentially expressed genes were identified by Significance Analysis of Microarrays (SAM) evaluation and subsequently screened for signaling pathway involvement. DNA extracts from the scalp biopsies were further examined using quantitative polymerase chain reaction (qPCR) for selected genes. Both LPP and PPB exhibited significant differential expression profiles compared to the intra-control scalp skin. Categorization of significantly differentially expressed genes by function indicated multiple functional pathways activated in both LPP and PPB including negative regulation of cellular and physiological processes, response to DNA damage stimulus, and cell death. However multiple gene function categories including, chemotaxis and inflammatory response, were uniquely identified in LPP as compared to PPB. The qPCR results from 3 selected genes (MMP11, TNFSF13B, APOL2) showed increased expression in LPP compared to PPB and MMP11 expression was confirmed in disease affected hair follicles by immunohistology. Though PPB is regarded by some as the end stage of LPP, we found relatively little evidence to support this view. While common gene function categories are represented in LPP and PPB, the results indicate they each exhibit distinct, active gene expression profiles suggesting they have unique biological identities. This information may help to establish appropriate, and effective, treatment protocols for these diseases.